

Claim 10 has been objected because it refers to amino acid sequences of Figures without references to the SEQ ID NOs. Claim 10 has been amended to correct the typographical omissions and reference the SEQ ID NOs. Support for the amendment to this claim may be found in the paper submitted on June 17, 2002, in response to "Restriction Requirement." Additional support may be found in the "Sequence Listing" previously submitted in this case. No new matter has been added by this amendment.

In light of the foregoing, Applicants request the reconsideration and withdrawal of the objections to the claims.

REMARKS

Claims 3, 7-17 and 22 are pending in this application. Claims 8 and 9 have been canceled without prejudice or disclaimer. New Claims 30-32 have been added in this Amendment.

Claim 30 has been added to recite specific amino acid substitutions. Support for new Claim 30 may be found in original Claim 8 and in the Specification at page 5, lines 30-31; page 6, lines 1-8; page 36, lines 16-22; page 37, lines 1-8; page 38, lines 1-7 and lines 18-20; and page 40, lines 1-5. Applicants thank the Examiner for the suggestion of reciting specific amino acid substitutions at the recited positions.

Claim 31 has been added and depends from new Claim 30. Support for new Claim 31 may be found in original Claim 9 and in the Specification at page 37, lines 18-21 and Figure 5 C (SEQ ID NO: 23).

Claim 32 has been added as an independent claim, as suggested in the Office Action. Support for new claim 32 may be found in original claims 10 and 11 and in the Specification at beginning on page 47, line 29, ending on page 48, line 2.

Claim Rejections – 35 USC §112:

Claims 3, 7-17 and 22 are rejected under 35 USC §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter applicant regards as the invention.

The instant Office Action states that Claim 3 is directed to a "non-naturally occurring IA protein comprising a substitution" and further points out that there is no structural starting point from which to make the substitutions. The Action also states there is lack of antecedent basis for the positions "B4-Y" and "B4-F."

Without admitting the propriety of the rejection, Claim 3 has been amended to include a structural reference source for the substitutions. Support for the amendment may be found in original claim 1 and in the Specification at page 2, lines 12-13; page 5, lines 16-23; page 6, lines 25-29 and Figure 1B.

The instant Action states that Claims 7 and 8 are also directed to "non-naturally occurring IA protein[s]" comprising substitutions where there is no structural starting point from which to make the substitutions. Without admitting the propriety of the rejection, Claim 7 has been amended to clarify the starting structure to which the substitutions are made. Claim 8 has been canceled making the rejection moot.

The Office Action states that Claims 3, 8, and 10 recite "IA protein" which is indefinite since this term is not recognized in the art and the specification fails to provide a positive recitation of structure for this term. Applicants respectfully disagree and submit the MPEP §2111.01 allows the Applicant to be their own lexicographer. Applicants respectfully draw the Examiner's attention to the disclosure of the meaning of "IA protein" as used in the claims. Furthermore, Applicants submit that a person of experience in the field of the invention would understand the term. See Specification at page 5, lines 17-23; and lines 24-27; page 9, lines 23-32; beginning on page 23, line 24, ending on page 24, line 3; page 27, lines 5-8; page 27, lines 14-17, and lines 18-32. Without admitting the propriety of the rejection, Claims 3 and 10 have been amended to recite "insulin activity" thereby clarifying the term.

Applicants respectfully request the reconsideration and withdrawal of the rejection of the claims in light of the above-amendments to the claims.

Claim Rejections – 35 USC §102(b):

Claim 8 is rejected under 35 USC 102(b) as being anticipated by Brange et al. (US Patent Number 5,618,913). Without admitting the propriety of the rejection, Applicants submit that Claim 8 has been canceled thereby making this rejection moot. Applicants respectfully request the withdrawal of the rejection in light of the foregoing amendment to the claims.

The Applicants submit that in light of the above-amendment and argument, the claims are now in condition for allowance and an early notification of such is respectfully solicited. Attached hereto is a marked-up version of the changes made to the Specification and Claims by the "Amendment". The attached page captioned "Appendix of Pending Claims" has been attached for the Examiner's

convenicncc. Please direct any calls in connection with this application to the undersigned at (626) 737-8040.

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APPENDIX OF PENDING CLAIMS

3. (Currently Amended) A non-naturally occurring insulin activity (IA) protein comprising an amino acid substitution of at least one amino acid residue when compared to the amino acid sequence of (SEQ ID NO: 2) and wherein said substitution is selected from B4-Y and B4-F.

7. (Currently Amended) A non-naturally occurring insulin activity (IA) protein comprising an amino acid substitution of at least one amino acid residue when compared to the amino acid sequence of (SEQ ID NO: 2) and wherein said substitution is selected from the group of B5-F, B5-W, B14-F, B14-W, B14-Y, and B14-I.

8. (Canceled)

9. (Canceled)

10. (Currently Amended) A non-naturally occurring IA protein, wherein said IA protein comprises an amino acid sequence selected from the group of amino acid sequences shown in Figure 3A (SEQ ID NO: 7), Figure 3B (SEQ ID NO: 8), Figure 3C (SEQ ID NO: 9), Figure 3D (SEQ ID NO: 10), Figure 3E (SEQ ID NO: 11), Figure 3F (SEQ ID NO: 12), Figure 3G (SEQ ID NO: 13), Figure 4A (SEQ ID NO: 14), Figure 4B (SEQ ID NO: 15), Figure 4C (SEQ ID NO: 16), Figure 4D (SEQ ID NO: 17), Figure 4E (SEQ ID NO: 18), Figure 4F (SEQ ID NO: 19), Figure 4G (SEQ ID NO: 20), Figure 5A (SEQ ID NO: 21), Figure 5B (SEQ ID NO: 22), and Figure 5C (SEQ ID NO: 23).

11. (Previously Amended) A recombinant nucleic acid encoding the non-naturally occurring IA protein of claim 10.

12. An expression vector comprising the recombinant nucleic acid of claim 11.

13. A host cell comprising the recombinant nucleic acid of claim 11.

14. A host cell comprising the expression vector of claim 12.

15. A method of producing a non-naturally occurring IA protein comprising culturing the host cell of claim 13 under conditions suitable for expression of said nucleic acid.
16. The method according to claim 15 further comprising recovering said IA protein.
17. (Previously Amended) A pharmaceutical composition comprising an IA protein according to claim 10 and a pharmaceutical carrier.
22. A non-naturally occurring IA protein according to claim 10 wherein said IA protein comprises the amino acid sequence shown in Figure 3A (SEQ ID NO: 7).
30. (NEW) A non-naturally occurring insulin activity (IA) protein comprising amino acid substitution compared to (SEQ ID NO: 2), wherein said substitutions are selected from the group consisting of A1N, A10Q, A16Y, A17Y, A17L, A17W, A17Q, A19F, B1D, B2E, B2T, B2K, B2Q, B2D, B2R, B2N, B2F, B4Y, B4F, B4E, B4K, B4R, B8L, B8L, B8K, B8E, B11I, B12R, B12K, B14F, B14W, B14Y, B14I, B14E, B14R, B14K, B14L, B25N, B26F, B27D, B28N, and B28F.
31. (NEW) The non-naturally occurring IA protein according to claim 30, wherein said substitutions are selected from the group of substitutions consisting of A1-N, A10-Q, A16-Y, A17-Y, A19-F, B1-D, B2-K, B4-F, B8-L, B11-I, B12-R, B14-W, B25-N, B26-F, B27-D, and B28-N.
32. (NEW) A recombinant nucleic acid encoding the non-naturally occurring IA protein selected from the group consisting of (SEQ ID NO: 7), (SEQ ID NO: 8), (SEQ ID NO: 9), (SEQ ID NO: 10), (SEQ ID NO: 11), (SEQ ID NO: 12), (SEQ ID NO: 13), (SEQ ID NO: 14), (SEQ ID NO: 15), (SEQ ID NO: 16), (SEQ ID NO: 17), (SEQ ID NO: 18), (SEQ ID NO: 19), (SEQ ID NO: 20), (SEQ ID NO: 21), (SEQ ID NO: 22), and (SEQ ID NO: 23).